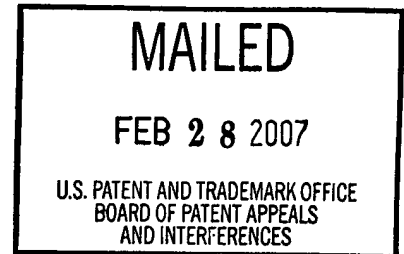


The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte MARIE HARRAS,
GREGORY DONOHO,
C. ALEXANDER TURNER JR.,
MICHAEL C. NEHLS,
GLENN FRIEDRICH,
BRIAN ZAMBROWICZ, and
ARTHUR T. SANDS



Appeal 2007-0528
Application 09/703,253
Technology Center 1600

ON BRIEF

Before SCHEINER, GRIMES, and LEOVITZ, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal involves claims to nucleic acids, which the Examiner has rejected for lack of patentable utility. We have jurisdiction under 35 U.S.C. § 134. We reverse.

BACKGROUND

The specification discloses “human polynucleotides encoding proteins that share sequence similarity with mammalian transporter proteins.” (Page 1.) More specifically, the encoded proteins “share structural similarity with mammalian multi-drug resistance (MDR) proteins and cellular transporters.” (*Id.* at 2.) One of the proteins has the sequence of 1219 amino acids shown in SEQ ID NO:24. (*Id.*) The disclosed proteins are said to be useful because, among other things, they “can be targeted (by drugs, oligos, antibodies, etc[.]) in order to treat disease, or to therapeutically augment the efficacy of, for example, chemotherapeutic agents used in the treatment of breast or prostate cancer.” (*Id.* at 14.)

DISCUSSION

1. CLAIMS

Claims 1 and 5-7 are pending and on appeal. Claim 5 is the broadest claim on appeal and reads as follows:

5. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO:24.

2. UTILITY

Claims 1 and 5-7 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, for lack of patentable utility. The Examiner argues that the specification does not disclose any specific and substantial utility for the claimed nucleic acids because it does not describe the function or biological significance of the encoded protein. (Answer 3-4.)

Appellants argue that the specification describes the proteins encoded by the claimed nucleic acids as transporter proteins, identifies the role of transporter proteins in drug resistance, and asserts a utility for the encoded proteins in increasing the efficacy of therapeutic agents used in cancer therapy. (Br. 5-6.) Appellants also rely on post-filing date evidence that shows that SEQ ID NO:24 is very similar to “ATP-binding cassette, subfamily C, member 11” or ABCC11. (*Id.* at 5.) Appellants argue that the post-filing evidence shows that ABCC11 is likely to be involved in multi-drug resistance and therefore confirms the utility asserted in the specification for SEQ ID NO:24. (*Id.* at 7-8.)

The Examiner argues that the post-filing references do not support the utility of the claimed nucleic acids because the proteins described in the references “have a stretch of approximately 160 additional amino acids not found in SEQ ID NO:23 [sic, SEQ ID NO:24].” (Answer 5.) The Examiner argues that as a result, and because “the art acknowledges that function cannot be predicted solely on structural similarity,” the protein of SEQ ID NO:24 would not be expected to have the same function as the proteins described in the post-filing references. (*Id.*)

The examiner bears the initial burden of showing that a claimed invention lacks patentable utility. *See In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (“Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide

rebuttal evidence sufficient to convince such a person of the invention's asserted utility."'). Here, the Examiner met his initial burden by presenting a reasonable explanation of why those skilled in the art would doubt the accuracy of the asserted utility based on the description of the invention in the specification.

Appellants, however, presented evidence intended to rebut the Examiner's rejection. Appellants' evidence became available only after the filing date of the instant application. Utility is determined as of the filing date of the application, *Brana*, 51 F.3d at 1567 n.19, 34 USPQ2d at 1441 n.19, and therefore post-filing evidence can be relied on only to support an assertion in the specification, not to add substantively to the specification's disclosure. *See In re Hogan*, 559 F.2d 595, 605 n.17, 194 USPQ 527, 537 n.17 (CCPA 1977) (later-published reference is acceptable as evidence of, for example, the accuracy of a statement in the specification).

Here, the specification states that the protein of SEQ ID NO:24 is similar in sequence to multi-drug resistance proteins (page 2). The specification also asserts a specific utility that appears to derive from the similarity of SEQ ID NO:24 to a group of proteins having a known function: increasing the efficacy of chemotherapy by inhibiting the protein of SEQ ID NO:24 (page 14).

In this case, we conclude that Appellants' references are evidence of the accuracy of statements made in the specification and therefore acceptable even though published after the filing date. Appellants have presented sequence comparisons, based on post-filing references, to show that SEQ ID NO:24 is very similar to a protein referred to as ABCC11.

(Ex. A and B attached to the Appeal Brief.) Appellants also cite Tammur,¹ Yabuuchi,² and Turriziani³ as evidence that ABCC11 would reasonably be expected to be involved in multi-drug resistance. (Br. 7-8)

We agree with Appellants that the post-filing evidence would lead those skilled in the art to reasonably expect that ABCC11 plays a role in multi-drug resistance. Tammur states that the “amino acid sequence of ABCC11 is 40% identical to human ABCC5 protein [and] 33% identical to ABCC4.” (Page 93, left-hand column.) Tammur also states that the “ABCC4 and ABCC5 proteins confer resistance to nucleotide analogs, including PMEA and purine base analogs. . . . Since structurally related ABC proteins often transport similar substrates across cell membranes, it would be reasonable to suggest that ABCC11 . . . could share functional similarities with ABCC4 and/or ABCC5.” (Page 93, right-hand column.)

In addition, Turriziani discloses that cells that are resistant to the toxic effect of a nucleoside analog (2',3'-dideoxy-3'-thiacytidine, or 3TC) show increased expression of ABCC11. (Abstract.) Turriziani states that its results “are most consistent with the concept that 3TC resistance is mediated by an inability to adequately accumulate 3TC. . . . It is possible that

¹ Tammur et al., “Two new genes from the human ATP-binding cassette transporter superfamily, ABCC11 and ABCC12, tandemly duplicated on chromosome 16q12,” *Gene*, Vol. 273, pp. 89-96 (2001).

² Yabuuchi et al., “Multiple splicing variants of two new human ATP-binding cassette transporters, ABCC11 and ABCC12,” *Biochem. Biophys. Res. Comm.*, Vol. 288, pp. 933-939 (2001).

³ Turriziani et al., “Impaired 2',3'-dideoxy-3'-thiacytidine accumulation in T-lymphoblastoid cells as a mechanism of acquired resistance independent of multidrug resistant protein 4 with a possible role for ATP-binding cassette C11,” *Biochem. J.*, Vol. 368, pp. 325-332 (2002).

increased ABCC11 expression decreases 3TC accumulation and increases cellular 3TC resistance.” Page 331, right-hand column. Turriziani also notes that the involvement of ABCC11 in 3TC resistance could not be directly confirmed at that time, and that the results could also be due to “a combination of increased MRP4 and ABCC11.” (*Id.*)

Although Appellants’ references do not unequivocally state that ABCC11 is involved in resistance to toxic drugs such as nucleoside analogs, they provide evidence of such involvement. We conclude that those of skill in the art would conclude that ABCC11 is reasonably likely to have utility based on its involvement in mediating cellular resistance to nucleoside analogs.

The instant claims, however, are not directed to nucleic acids encoding ABCC11. They are directed to nucleic acids encoding SEQ ID NO:24. As the examiner has pointed out, the amino acid sequences of ABCC11 and SEQ ID NO:24 differ in that ABCC11 includes a stretch of about 160 contiguous amino acids that is missing from SEQ ID NO:24. The question to be addressed, then, is whether this difference in amino acid sequence would be expected to result in a difference in function.

The Examiner has asserted that this deletion precludes those skilled in the art from concluding that the two proteins would share the same function. (Answer 5.) The Examiner has cited several references as evidence that “function cannot be predicted based solely on structural similarity to a protein.” (*Id.*, citing the Office action mailed Dec. 19, 2001, which in

turn cites several prior art references.) The Examiner characterizes some cited references as showing that, in some “polypeptide families . . . individual members have distinct, and sometimes even opposite, biological activities.” (Office action mailed Dec. 19, 2001, page 5.) The Examiner characterizes other references as showing that database annotations are unreliable. (*Id.*, page 6.)

The Examiner’s references are entitled to less weight than Appellants’. While it may be true in some polypeptide families that sequence similarity does not accurately predict functional similarity, that apparently does not apply here. Tammur specifically states that “structurally related ABC proteins often transport similar substrates across cell membranes,” and concludes that “it would be reasonable to suggest that ABCC11 . . . could share functional similarities with ABCC4 and/or ABCC5.” (Page 93, right-hand column.) The Examiner’s references, which discuss other protein families, are less probative than Appellants’ evidence directed specifically to the ABC family of proteins.

Similarly, we do not find the Examiner’s database-related references to outweigh Appellants’ evidence. Even if some database annotations cannot be relied on, the evidence provided by the Tammur, Yabuuchi, and Turriziani references persuasively shows that those skilled in the art recognized ABCC11 as a member of the family of ATP-binding cassette transporter proteins and considered ABCC11 reasonably likely to be involved in transport of nucleoside analogs.

The relevant question is whether the structural difference between ABCC11 and SEQ ID NO:24 – a 160 amino acid deletion – would be likely to result in a difference in function. The Examiner has provided no evidence or scientific explanation to establish that SEQ ID NO:24 would not share the same function as ABCC11. The Examiner has not, for example, established that the deleted region includes one of the two ATP-binding cassette domains shown in Tammur's Figure 2 or any of the labeled motifs shown in Tammur's Figure 1.

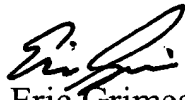
When a *prima facie* case of unpatentability has been made out and evidence has been submitted in rebuttal, the examiner must take a step back and re-evaluate patentability based on the totality of the evidence. *See In re Rinehart*, 531 F.2d 1048, 1052, 189 USPQ 143, 147 (CCPA 1976). Patentability is determined based on a preponderance of the evidence. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Here, we conclude that the weight of the evidence supports the specification's statement that the protein of SEQ ID NO:24 would reasonably be expected to be useful in increasing the efficacy of cancer chemotherapy. The rejections under 35 U.S.C. § 101 and 112, first paragraph, for lack of utility are reversed.

Since we conclude that the claimed products are supported by at least one patentable utility, we need not consider whether the other utilities asserted by Appellants (Br. 9-17), which do not depend on the specific properties of SEQ ID NO:24, would meet the standard of 35 U.S.C. § 101.

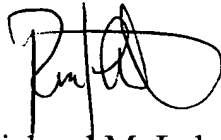
REVERSED



Toni R. Scheiner)
Administrative Patent Judge)



Eric Grimes)
Administrative Patent Judge)



Richard M. Lebovitz)
Administrative Patent Judge)

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) APPEALS AND
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) INTERFERENCES
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EBG/jlb

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